

Case Report

Intraperitoneal administration of paclitaxel combined with S-1 plus oxaliplatin followed by conversion surgery in a patient with stage IV gastric cancer and intestinal malrotation: Report of a case.

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Abstract

Background: The prognosis of patients with stage IV gastric cancer remains unsatisfactory despite recent advances in multidisciplinary therapy. Asymptomatic intestinal malrotation in adults is rare and usually diagnosed incidentally by imaging or during abdominal surgery. Intestinal malrotation associated with primary gastric cancer is extremely rare. We report here a patient with stage IV gastric cancer and intestinal malrotation successfully treated with induction chemotherapy followed by gastrectomy.

Case presentation: The patient is a 57-year-old woman diagnosed with gastric cancer with peritoneal metastases. Staging laparoscopy showed disseminated nodules on the peritoneal surface with a peritoneal cancer index score of 15 points. Peritoneal fluid cytology was class V. The patient was treated with intraperitoneal administration of paclitaxel combined with S-1 plus oxaliplatin. After twelve courses of combined chemotherapy, 2nd look laparoscopy showed that peritoneal metastases were not macroscopically present and cytological examination of peritoneal washing fluid was negative for malignant cells. Total gastrectomy with regional lymph node dissection was then performed. Pathological examination of the specimen revealed grade 1b efficacy of IP-PTX plus SOX chemotherapy. She also had the non-rotation type of malrotation. Anatomical anomalies could cause difficulties for lymph node dissection and reconstruction during the gastrectomy against gastric cancers. The postoperative course was uneventful. Following resection, the patient received 14 courses of the same combined chemotherapy without oxaliplatin. She has done well for more than 6 months after resection without evidence of recurrence.

Discussion: This is the first report of successful conversion surgery for a patient with stage IV gastric cancer and intestinal malrotation after intraperitoneal administration of paclitaxel combined with S-1 plus oxaliplatin. Gastrectomy performed after an excellent response to combined chemotherapy of peritoneal metastases may contribute to improved patient outcomes. Establishing the diagnosis of intestinal malrotation preoperatively in adults is necessary to safely perform abdominal surgery.

(Keywords: Administration of paclitaxel, Case report, Conversion Surgery, Intraperitoneal Intestinal malrotation, Stage IV gastric cancer)

Background

The incidence of gastric cancer and the mortality of patients with this disease have decreased worldwide over

the past several decades^[1]. However, gastric cancer remains a major public health issue as the fifth most common cancer and the fourth leading cause of cancer death^[2]. The

peritoneal cavity is the most frequent site for metastases from gastric cancer and of recurrences in patients with advanced gastric cancer^[3]. Patients who present with peritoneal metastases are generally treated with systemic chemotherapy without curative surgery^[4].

The development of new chemotherapeutic and molecular targeting agents has led to new approaches such as neoadjuvant chemotherapy followed by conversion surgery being introduced as a novel strategy to improve the outcome of patients with stage IV gastric cancer^[5]. We have previously reported the efficacy of intraperitoneal administration of paclitaxel (IP-PTX) combined with S-1 plus oxaliplatin (SOX) treatment as induction chemotherapy for patients with gastric cancer with peritoneal metastases^[4].

Intestinal malrotation, a congenital anomaly, is caused by incomplete rotation of the embryonic midgut^[6]. It is generally diagnosed in children, especially with the development of complications such as midgut volvulus or closed-loop obstruction from internal hernias^[7]. Intestinal malrotation detected in asymptomatic adults is very rare and is usually an incidental finding on imaging studies or during abdominal surgery^{[6][7]}. Anatomical anomalies could lead to difficulties in lymph node dissection and reconstruction after gastrectomy in patients with gastric cancer. Successful conversion surgery for a patient with stage IV gastric cancer and intestinal malrotation following intraperitoneal neoadjuvant chemotherapy is reported here.

Case presentation

A 57-year-old woman was referred with advanced gastric cancer. Upper gastrointestinal endoscopy showed a type 4 lesion in the middle to lower body of the stomach (Fig. 1). Biopsy revealed poorly differentiated adenocarcinoma with signet ring formation. Contrast-enhanced computed tomography (CT) scan showed thickening of the wall of the stomach and ascites (Fig. 2a) without metastases to the liver or paraaortic lymph nodes. A superior mesenteric vein rotation sign was incidentally noted, consistent with intestinal malrotation (Fig. 2b). Staging laparoscopy showed disseminated nodules on the peritoneal surface of the abdominal cavity with a peritoneal cancer (Fig. 3) index score of 15 points. Peritoneal fluid cytology was class V. Tumor stage (UICC 8th edition) was T4aN1M1 (peritoneum), stage IV. At the end of staging laparoscopy, an intraperitoneal access port was placed for administration of intraperitoneal chemotherapy. After staging laparoscopy, the patient received IP-PTX combined with SOX chemotherapy. Oxaliplatin was administered intravenously at 100 mg/m² on day 1, S-1 was administered orally twice daily at 80 mg/m² per day for 14 consecutive days, followed by 7 days without treatment. On days 1 and 8, paclitaxel 40 mg/m² (maximum 60 mg) was diluted in 1 L of saline at room temperature and administered intraperitoneally using the access port over 2 hours. This chemotherapy regimen was approved as a clinical study by the Institutional Review Board of Jichi Medical University, and written informed consent was

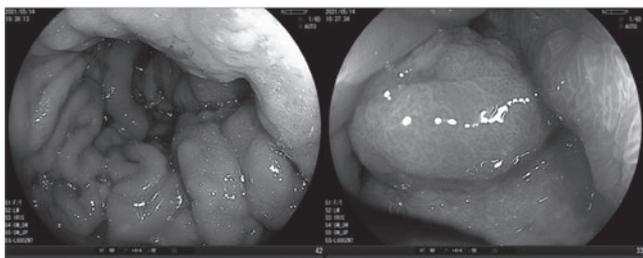


Figure 1. Endoscopic findings.

Upper gastrointestinal endoscopy showed a type 4 malignant lesion in the middle to lower body of the stomach.

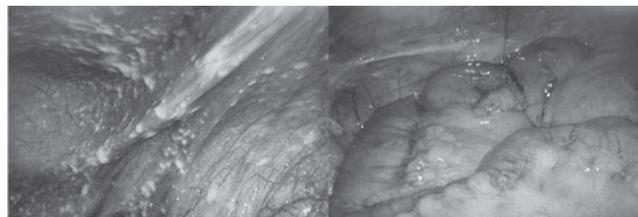


Figure 3. Staging laparoscopy findings.

Staging laparoscopy showed disseminated nodules on the peritoneal surface in the abdominal cavity.

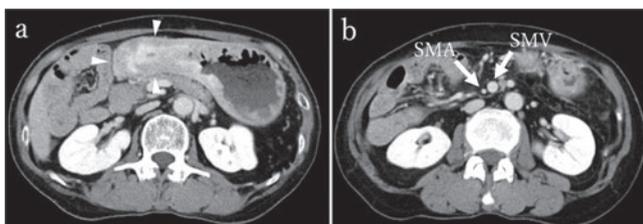


Figure 2. Computed tomography (CT) scan findings before treatment.

2a. Contrast-enhanced CT scan showed thickening of the wall of the stomach with ascites.

2b. A superior mesenteric vein rotation sign was noted, consistent with non-rotation type of intestinal malrotation.

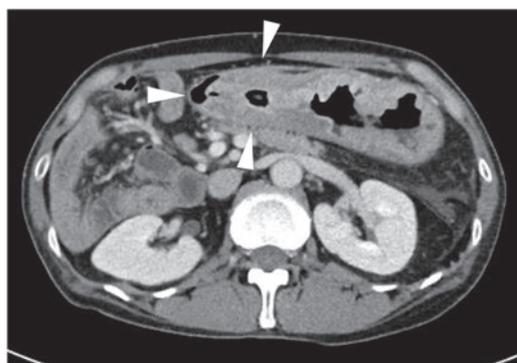


Figure 4. Computed tomography (CT) scan findings after induction chemotherapy.

After twelve courses of combined chemotherapy, CT scan showed reduced gastric wall thickening.

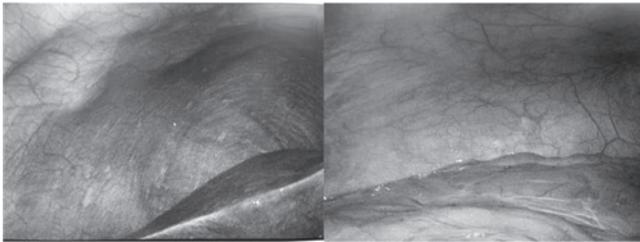


Figure 5. Findings at the second laparoscopy.

A second laparoscopy showed that peritoneal metastases were not macroscopically present.

obtained from the patient.

After 12 courses of combined chemotherapy, CT scan showed reduced gastric wall thickening, and disappearance of ascites (Fig. 4). Liver metastases or paraaortic lymph node metastases were not seen. A 2nd look laparoscopy showed no evidence of macroscopic peritoneal metastases (Fig. 5). Cytological examination of peritoneal washings obtained during laparoscopy was negative for malignant cells. After a total of 12 courses of combined chemotherapy, total gastrectomy with regional lymph node dissection was performed. We had a one-month period of chemotherapy withdrawal before and after the surgery. The patient also had non-rotation type of malrotation, with the small intestine on the right side and the colon on the left side. Since there was no Ladd's ligament, we did not perform Ladd's operation. Roux-en-Y reconstruction with closure of the defect between the Roux limb and retroperitoneum were performed to prevent future internal herniation. There were no intraoperative difficulties due to the presence of intestinal malrotation, because this congenital anomaly was diagnosed preoperatively.

Pathological examination of the specimen revealed grade 1b efficacy of IP-PTX combined with SOX chemotherapy, meaning that viable cancer cells remained in from one-third to two-thirds of the primary lesion (Fig. 6). The postoperative course was uneventful. After gastrectomy, the patient received 14 courses of the same combined chemotherapy without oxaliplatin. She has done well for more than six months postoperatively without evidence of recurrence.

Discussion

The prognosis of patients with stage IV gastric cancer is poor and remains unsatisfactory, while treatment with chemotherapy has recently shown great advances. The median overall survival of patients with stage IV gastric cancer is reported to be 13–16 months^{[8][9]}.

Several conversion therapy approaches have recently been used with some success in patients with stage IV gastric cancer^[10]. Okabe et al. described that limited peritoneal dissemination from primary gastric cancer is highly

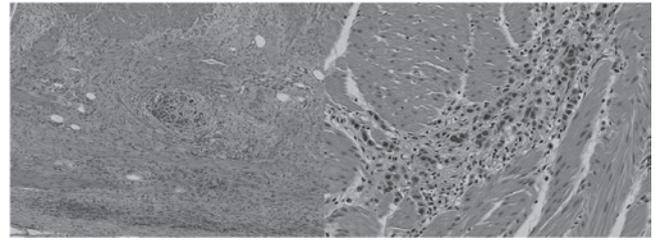


Figure 6. Pathological findings. (Hematoxylin and eosin stain).

The resected specimen showed a grade 1b response of gastric cancer cells to induction chemotherapy.

sensitive to induction chemotherapy and conversion surgery after resolution of peritoneal metastases could result in cure in some patients^[11]. Induction chemotherapy followed by conversion surgery may contribute to an improved prognosis in some patients with stage IV gastric cancer. "Conversion surgery" is defined as surgical treatment with the goal of an R0 resection after neoadjuvant chemotherapy for tumors that were originally unresectable or marginally resectable for technical and/or oncologic reasons^[5].

We reported previously that combination chemotherapy using the IP-PTX combined with SOX regimen is highly effective and is recommended as induction chemotherapy for patients with peritoneal metastases from gastric cancer^[4]. We believe that IP-PTX can be an important element in the treatment of patients with gastric cancer with peritoneal metastases to improve the generally poor outcomes. When PTX is administered intraperitoneally, it is expected to maintain a high concentration in the peritoneal cavity due to its pharmaceutical characteristics, being hydrophobic with a high molecular weight and elicit notable antitumor activity against peritoneal metastases with less systemic toxicity^[12]. Thus, IP-PTX has a pharmacokinetic advantage to control peritoneal lesions and can be combined with various systemic chemotherapeutic agents^[13]. Based on these findings, a combined chemotherapy approach for repeated administration of IP-PTX using an implantable port system together with systemic chemotherapy was introduced^[14]. In our study, the 1-year overall survival (OS) rate was 79.5% (95% CI 64.4-88.8%) with a median survival time of 25.8 months^[4]. Conversion surgery was performed in 45% of patients who had macroscopic diminution of peritoneal metastases with a 1-year OS rate of 100% (95% CI 69.5-100%)^[4].

The present patient had no distant metastases except for peritoneal disseminated disease detected by clinical routine examinations, which is considered category 3 according to the new biological categories for the classification of stage IV gastric cancer^[10]. Category 3 patients with stage IV gastric cancer reportedly have the longest mean survival time after treatment with conversion surgery after chemotherapy among the four categories^[15]. Conversion

gastrectomy following induction chemotherapy such as IP-PTX combined with SOX could have a significant role to improve the prognosis of patients with stage IV gastric cancer with peritoneal metastases. With the benefit of this new strategy, the present patient has no evidence of recurrence 18 months after initial treatment.

Asymptomatic intestinal malrotation was detected incidentally by preoperative CT scan in this patient. Intestinal malrotation is a rare congenital anomaly referring to incomplete rotation of the primitive midgut around the superior mesenteric artery (SMA) during fetal development^[16]. The incidence of malrotation in adults is rare, estimated to be approximately 0.2% of the population^[16]. Wang categorized intestinal malrotation into four groups including non-rotation with incomplete 90° rotation, malrotation with 180° rotation, reversed rotation, and paraduodenal hernia^[17]. This patient was classified as the non-rotation type because the small bowel was found on the right side and the colon on the left side without a ligament of Treitz. Rarely, malrotation is first identified adulthood^[18]. Reconstruction performed following gastrectomy in patients with intestinal malrotation could lead to difficulties when performing standard procedures^[16]. The present patient had neither a ligament of Treitz nor the jejunum on the left side. The right-sided colon was completely mobilized to the left-side of the abdomen. In general, either an ante-colic or retro-colic route for a Roux-en-Y reconstruction can be selected after total gastrectomy. Since the transverse-colon was not in its usual position, the defect between the Roux-en-Y limb and retroperitoneum was closed to prevent possible internal herniation. Patients with intestinal malrotation also have adhesions from the pancreatic head to the first part of the duodenal wall^[6]. This could increase the risk of injury to the pancreatic head during the dissection around the left gastroepiploic vessels. The procedure performed for the lymph node dissection in the infrapyloric area led to avoiding this injury as the presence of intestinal malrotation was known.

Intestinal malrotation associated with primary gastric cancer is extremely rare. It is very important to establish the preoperative diagnosis for this anatomical variance to prevent unexpected difficulties during surgery.

The present patient had asymptomatic intestinal malrotation as well as stage IV gastric cancer.

To the best of our knowledge, this is the first report of successful conversion surgery for a patient with stage IV gastric cancer and intestinal malrotation after receiving IP-PTX combined with SOX chemotherapy, while the intestinal malrotation has nothing to do with the efficacy of IP-PTX chemotherapy. It is hoped that conversion surgery after receiving neoadjuvant IP-PTX combined with SOX therapy will improve her long term prognosis.

Conclusion

In conclusion, IP-PTX combined with SOX can be used in a neoadjuvant fashion for the treatment of patients with peritoneal metastases from gastric cancer. Gastrectomy performed after an excellent response of the peritoneal metastases may contribute to improved patient outcomes. Preoperative diagnosis of intestinal malrotation is important to perform safe gastrectomy and reconstruction.

Declarations of interest

The authors declare that they have no conflict of interest.

List of Abbreviations

Intraperitoneal Paclitaxel: IP-PTX

S-1 plus Oxaliplatin: SOX

Ethics approval and consent to participate

Not applicable.

Consent for publication

Informed consent for the publication of this case report was obtained from the patient.

Availability of data and materials

Not applicable.

Competing interests

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Author's contributions

KF, SS, RK, KK, YH, HO and HY were engaged in the patient's care including the surgery, chemotherapy and prepared the manuscript. SS, NS, JK and AL helped in drafting the manuscript and interpretation. NS and TN contributed the pathological diagnosis. All authors have read and approved the final manuscript for publication.

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腸回転異常症を伴う胃癌腹膜播種に対し，パクリタキセル腹腔内投与併用化学療法後，Conversion Surgeryを施行しえた1例

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要 約

当院では，2016年1月より腹膜播種陽性胃癌を対象に，パクリタキセル腹腔内投与併用化学療法を導入し，腹膜播種奏功例に対してはConversion Surgeryを行っている。症例は57歳，女性。胃癌術前検査で腹膜播種を疑い，審査腹腔鏡を施行した。播種結節を認めP1, PCI score 15点，腹水細胞診class Vであった。pT4aN1M1 (PER) pStage IVと診断し，腹腔ポートを造設，SOX+腹腔内PTX投与を開始した。SOX+IP-PTX 12コース施行後に2nd look審査腹腔鏡を行い，CY0P0であった。R0切除可能と判断し，Conversion Surgeryとして開腹胃全摘術を施行した。本症例は腸回転異常症を伴っていた。胃癌手術で腸回転異常により定型手術が行えず，難渋した報告がある。本症例は腸回転異常を伴う胃癌腹膜播種に腹腔内化学療法が奏功し，Conversion Surgeryを施行しえた初めての報告である。腸回転異常症の術前診断は重要であり，化学療法による腹膜播種奏功例ではConversion Surgeryが予後改善に寄与する可能性がある。

(キーワード：パクリタキセル，症例報告，Conversion Surgery，腸回転異常症，Stage IV胃癌)